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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SALVOZA, M FRANCO G	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,029	DESPRES ET AL.	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *4-12, 14-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant has elected Group I drawn to claims 1-3 and 13 with traverse. Applicant has elected Group I requesting that all the claims be rejoined since they do not impose a serious search burden.

Applicant's arguments are considered but are unpersuasive. The claims are drawn to patentably distinct inventions, such as a peptide, polynucleotide, antibodies, and attenuated strains in addition to methods of using and preparing said compositions and products. These inventions have patentably distinct structures, functions and properties requiring separate searches of the prior art as evidenced by their separate classification which would create an undue burden on the examiner.

The restriction is maintained and made FINAL.

Claims 1-3 and 13 are pending and under consideration. Since part of claim 13 is drawn to a nonelected invention, only the relevant part will be examined. The inventions are distinct, and the first part reciting the composition and at least one pharmaceutically acceptable carrier will be examined but not the polynucleotide encoding the same or a polynucleotide encoding an attenuated flavivirus strain according to claims 4 to 6. Applicant is reminded that restriction between products that do not share a common utility and share a substantial structural feature essential to that utility is proper (emphasis added). See MPEP 803.02.

Claim Objections

Claim 13 is objected to under 37 CFR 1.75(c) as being in improper form because it contains language drawn to a multiply dependent claim by reciting "a peptide according to claims 1 to 3." See MPEP § 608.01(n). It is presumed the three claims are implied to be dependent in the alternative, however, appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 3 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 2 and 3 are drawn to isolated peptides that are selected in the group consisting of peptides of 6-9 amino acids wherein X5 represents F. This is vague and indefinite since places X1 and X2 are indicated in claim 1 to possibly be absent. If X1 and X2 are absent, would the F (phenylalanine) amino acid be in the original X5 position, or would the peptide be renumbered from the X3 position so that phenylalanine is located in five positions from X3 (X7)?

In addition, claim 3 is drawn to an isolated peptide according to claim 1 or 2, characterized in that said peptide "is associated with" or conjugated to another peptide or protein such as a carrier protein or non-peptide molecule and/or incorporated into a suitable support. The terms "associated with" and "incorporated into a suitable support" are vague and indefinite. "Associated with" can be interpreted as broadly as in the same composition or solution,

covalently linked, noncovalently linked, ionic bonded. Additionally, "incorporated into a suitable support" is a vague and indefinite term that can be interpreted in many ways.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 13 is drawn to a pharmaceutical composition comprising an effective amount for inducing protection against flavivirus infections of a peptide and at least one pharmaceutically acceptable carrier. The specification does not teach one how to use the invention in that one can use "an effective amount" of the peptide and composition to "induce protection against flavivirus infections." This rejection is based on the intended use of the composition to induce protection.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

> The breadth of the claims: Claim 13 very broadly recites "an effective amount to induce protection against flavivirus infection." While flaviviruses have in common positive, nonsegmented RNA, the genus encompasses as many as 70 subspecies of virus that have unique characteristics, from West Nile strains to Dengue strains to Japanese encephalitis virus strains. Examples are drawn to

specific strains of these separate species, yet likely would not be enabling for the entire breadth of the genus.

The state of the prior art: While improvements are being made in flavivirus vaccines, many challenges need to be met, such as: appropriate *in vivo* animal models in lieu of primates, avian, murine or equine models that would correlate sufficiently with human models; protection against reversions to wild type viruses; variation in serological tests and criteria for interpreting the efficacy of results; agreed upon dosages and subsequent boosts to immunity; and attenuation standards. ("Recent Advancement in Flavivirus Vaccine Development," Chang et al. *Expert Rev. Vaccines* 3(2), 2004.)

In addition to the lack of consistent success for the genus of flaviviridae as a whole, each species also creates unique challenges to ensuring and inducing sufficient protection. For example, Dengue virus itself poses a "considerable scientific challenge due to the disease being caused by four serologically related viruses. .. Lack of an animal model that reproduces the disease has limited our understanding of pathogenic mechanisms" ("Review on Flavivirus Vaccine development," *Vaccine* 23 (2005) 2689-2695).

The level of one of ordinary skill: Based on current protocols and the state of the prior art, one of ordinary skill in the art would be not sufficiently apprised of what would constitute "an effective amount to induce protection against flavivirus infection" due to the lack of consistent results that translate well to *in vivo* human models from animal models for the range of flavivirus species.

The level of predictability in the art: The state of the art is improving, yet there is not sufficient consistent correlation of treatments for the different types of flaviviruses from animal models to induce protection in humans. New approaches using DNA, chimeric and live attenuated vaccines have improved results for species such as West Nile and Dengue, yet a lack of agreed upon standards and results correlating to *in vivo* human models contribute to the lack of predictability in the art. "A major practical challenge on the path to a safe and efficacious DEN vaccine is the understanding of the mechanism of virus neutralization and the development of an in vitro assay that would be a meaningful surrogate for protection. This observation is corroborated by the finding that DEN candidate vaccine recipients developed clinical DEN fever with DEN viraemia, despite having pre-existing neutralizing antibodies to the virus. These findings underscore the need for additional research into protective immune mechanisms, including cell-mediated protection" (p. 2694, Id.).

The existence of working examples: The specification contains a limited set of three examples concerning expression of the M ectodomain leading to apoptosis for a Dengue virus isolate, proapoptotic properties of the m ectodomain of Japanese encephalitis, West Nile and Yellow Fever viruses in several WN, JE and DEN strains, and determination of a six-nine residue sequence required for the

induction of apoptosis by the M ectodomain. While applicant has proven correlation between specific ectodomains and loss of cytotoxicity in certain strains, the examples do not demonstrate enough data to reach the standard of "inducing protection against flavivirus infection."

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Based on a weighing of the previous factors, a high degree of experimentation would still be needed to determine what would constitute "an effective amount to induce protection" "against flaviviruses would be.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. § 102(b) as being anticipated by result "rat ninjurin peptide" peptide search result by Milbrandt et al. dated June 23, 1998, which is more than one year prior to applicant's filing date of June 3, 2003.

Claim 1 recites an isolated and purified peptide with the formula X1-X2-X3-X4-X5-X6-X7-X8-X9 wherein: X1 is absent or represents an amino acid selected in the group consisting of non-charged polar amino acids and non polar amino acids; X2 is absent or represents an amino acid selected in the group consisting of acidic amino acids, non-charged polar amino acids and nonpolar amino acids; X3 is selected in the group consisting of basic amino acids, non-charged

amino acids, non-charged polar amino acids and non-polar amino acids; X4 is W; X5 represents any amino acid except A, L or I; X6 is a non-polar amino acid; X7 is a basic amino acid; X8 is selected in the group consisting of basic amino acids and non-charged polar amino acids and; X9 is absent or represents an amino acid selected in the group consisting of basic amino acids and non-polar amino acids.

Milbrandt et al.'s rat ninjurin peptide has an absent amino acid in the X1 position, an absent amino acid in the X2 position, amino acid R (Arginine) from the group of basic amino acids at X3, amino acid W (Tryptophan) in the X4 position, amino acid G (Glycine) in the X5 position, amino acid L (leucine) from the non polar amino acid group in the X6 position, and amino acid R (Arginine) from the group of basic amino acids in the X7 position, amino acid N (Asparagine) from the non-charged polar amino acid group in position X8, and in X9 the amino acid R (Arginine) from the group of basic amino acids. This reference anticipates each of the peptide limitations of claim 1.

Claim 3 is rejected under 35 U.S.C. § 102(b) as being anticipated by Milbrandt et al.'s rat ninjurin peptide. Claim 3 is drawn to the isolated peptide of claim 1 characterized in that said peptide is associated with or conjugated to another peptide or protein such as a carrier protein or nonpeptide molecule and/or incorporated into a suitable support. The rat ninjurin peptide product is stated to be used for detection, purification, diagnosis and screening assays which would be incorporating the peptide into a solid support.

Claims 1, 2 and 13 are rejected under 35 U.S.C. § 102(a) as being anticipated by Skubitz et al.'s result "human CD66 family modulating peptide SEQ ID NO 101." Claim 2 recites an

isolated peptide characterized in that it is selected in the group consisting of peptides 6-9 amino acids wherein X5 represents F.

With respect to claim 13, intended use of "inducing protection against flavivirus" is not given patentable weight. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, the pharmaceutical composition of claim 13 requires a peptide according to any one of claims 1-3.

The Skubitz et al. "human CD66 modulating peptide SEQ ID NO 101" reference teaches an isolated peptide consisting of 6-9 amino acids (here, 8) wherein X5 represents F. X1 is absent; X2 is absent; X3 is R or (Arginine) from the group consisting of basic amino acids; x4 is W; x5 is F; x6 is F (phenylalanine), a nonpolar amino acid; x7 is K (lysine), a basic amino acid; X8 is noncharged polar amino acid N (Aspargine). This reference meets the limitations of claim 2 and was published Sept. 6, 2002, one year within applicant's effective date of filing. Skubitz et al. also teaches a peptide in a pharmaceutical composition that is administered in at least one pharmaceutically acceptable carrier. Skubitz et al. teaches the modulation of the function of CD44 family members and/or their ligands and treating and diagnosing autoimmune diseases, cancer, infections (e.g. bacterial or viral) or inflammatory diseases, in transplantation therapies and for immunization.

Claims 1 and 13 are rejected under 35 U.S.C. § 102(b) as being anticipated by Fraser et

al. (U.S. Patent No. 6180604.) Claim 13 recites a pharmaceutical composition comprising an effective amount for inducing protection against flavivirus infections of a peptide and at least one pharmaceutically acceptable carrier.

Fraser et. al., issued Jan. 30, 2001 which is more than one year before applicant's filing date of June 3, 2003, teaches a method of treating an infection, comprising administering to a patient a therapeutically effective amount of a pharmaceutical composition (column 3, line 45). The infection may be caused by, for example a microorganism, such as a bacterium, fungus, parasite or virus (column 4, line 7). Fraser et al. also teaches APS-modified peptides in pharmaceutically acceptable carriers in column 57, line 20 that contain the peptide sequence of WPWWPWRRK. This sequence falls within the scope of claim 1, since X1 represents W (tryptophan), a nonpolar amino acid; X2 represents P (proline), a nonpolar amino acid; X3 represents W(tryptophan), a nonpolar amino acid; X4 represents W(tryptophan); X5 represents P(proline); X6 represents W(tryptophan), a nonpolar amino acid; X7 represents R (Arginine), a basic amino acid; X8 represents R (Arginine), a basic amino acid; and X9 represents K (Lysine), a basic amino acid. Therefore, the Fraser et al. reference teaches the peptide in a pharmaceutically acceptable carrier in a pharmaceutical composition.

Double Patenting

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/608,147. Although the conflicting claims are not identical, they are not patentably distinct from each other because the group of amino acids in claim 1 of the present application is within the scope of the group of amino acids listed in claim 1 of Application No. 10/608,147.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Franco Salvoza
Patent Examiner

SHANON FOLEY
PRIMARY EXAMINER